

**REMARKS/ARGUMENTS**

Claims 1-12 are pending in this application. Claims 2-12 are rejected.

In response to the Examiner's statement that the oath or declaration is defective, because a non-initialed change had been made to the term "Noble", Applicants attach as Exhibit 1 a replacement declaration which cures the noted defect.

Applicants have amended the title to correspond to the title of parent application serial no. 09/023,731, now U.S. Patent No. 6,291,648 B1.

In response to the Examiner's objection to the specification that the trademark SOLR should be capitalized wherever it appears and be accompanied by the generic terminology, Applicants submit that the SOLR strain, as well as the SURE strain, and TOP strain are all E.coli host cell strains which have host names that are registered with the RIKEN Cell Bank, a well known depository organization in Japan.

Applicants attach as Exhibit 2 copies of pages from the RIKEN General Catalog, No. 4, published on April 1999 showing that the "SOLR", "SURE", and "TOP" strains are listed as host names, and providing information for each strain. Applicants have amended the paragraph of specification at page 6, beginning at line 25 to add the registration information. Applicants also added the SURE and TOP strains to the list of E.coli strains in the same amendment, as those strains were recited in claim 10 as part of the original disclosure. In addition, Applicants also amended the spelling of TOP in claim 10 to correct an inadvertent typographical error. Applicants respectfully submit that the amendments just described would clearly identify to one skilled in the art the host cells of the invention.

In response to the Examiner's objection to claims 2-12 as depending on a non-elected claim 1, Applicants have canceled claim 2, and re-presented it in independent form as claim 13. Claim 1 has been canceled. Claims 2 through 12 have also been amended to correct a typographical error (the word "molecule", has been changed to "molecule"), and to correct the pendency of the claims in view of the cancelation of claim 2. No new matter has been introduced by virtue of the canceled and amended claims.

**REJECTION OF CLAIMS UNDER 35 U.S.C. §112, second paragraph**

The Examiner rejected claims 4 and 10 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Specifically, the Examiner contends that claim 4 is indefinite for reciting "derived from Tricholoma matutake" because the exact meaning of the phrase is not clear. According to the Examiner, "it is not clear how the nucleic acid is "derived"". The Examiner further states, "Is the nucleic acid changed or altered or is the nucleic acid from Tricholoma matsutake?"

In response, Applicants submit that the amendment herein to claim 4 deleting the word "derived" overcomes the Examiner's §112, second paragraph rejection, because claim 4 now recites that the nucleotide molecule is from Tricholoma matsutake.

The Examiner also rejected claim 10 under §112, second paragraph, because Claim 10 contains the trademarks or trade names SOLR, SURE, TOPP.

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According to the Examiner, the claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product.

In response, Applicants respectfully submit that the amendment to the specification at page 6, in the paragraph beginning at line 25, overcomes the Examiner's §112, second paragraph, rejection, because the specification now makes clear that the host names SOLR, SURE, and TOP are host names given in the RIKEN depository in Japan. As stated above, Applicants attach as Exhibit 2, the relevant pages of the RIKEN catalog listing the SOLR, SURE, and TOP E.coli strains and providing product information for each strain. Therefore, Applicants submit that one skilled in the art would be able to properly identify the host cells of the invention based upon the reference to the RIKEN depository.

In view of the amendments and remarks presented above, Applicants respectfully request that the Examiner withdraw the rejections under §112, second paragraph.

**REJECTION OF THE CLAIMS UNDER 35 U.S.C. §112, first paragraph**

The Examiner rejected Claims 1-2 and 4-12 under 35 U.S.C. §112, first paragraph. According to the Examiner, the specification,

"while being enabling for the nucleic acid encoding the protein of Pestka (US Patent 6, 300,474) and a nucleic acid which encodes a protein comprising SEQ ID NO: 1, and a nucleic acid of SEQ ID NO: 2 and vectors and host cells comprising such nucleic acids and a method of preparing the protein encoded by said nucleic acids, [the specification] does not reasonably provide enablement for a nucleic acid which encodes a modified amino acid sequence of SEQ ID NO:1 which have antitumor

activity wherein one or more amino acids are added and/or inserted into SEQ ID NO: 1 and/or one or more amino acids are substituted and/or deleted in SEQ ID NO: 1 and pharmaceutical compositions comprising which is used as a antitumor agent."

The Examiner also contends that "the claims broadly encompass a nucleic acid which encodes a modified amino acid sequence consisting of SEQ ID NO:1 which have additions, insertions, substitutions, and deletions and which retain activity as well as in vitro and in vivo pharmaceutical compositions for use as antitumor agents", and the "claims also broadly read on a nucleic acid which encodes for a protein in which every residue of SEQ ID NO: 1 has been deleted or substituted." The Examiner concludes that in view of the unpredictability in protein chemistry (citing the prior art), "one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention."

In response, Applicants respectfully submit that the §112, first paragraph rejection is rendered moot by the cancelation of claim 2. Claim 13 which re-presents former dependent claim 2 in independent form does not recite modified amino acid sequences of SEQ ID NO.: 1; therefore, the Examiner's rejection no longer applies. Accordingly, Applicants respectfully request that the Examiner withdraw this ground of rejection.

The Examiner rejected Claim 9 under 35 U.S.C. 112, first paragraph, stating that "it is unclear if the cell lines COP-5 and C127 are known and publicly available, or can be reproducibly isolated from nature without undue experimentation." According to the Examiner, because "one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the

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availability of the claimed COP-5 and C127 cell lines, a suitable deposit for patent purposes, evidence of public availability of the claimed cells, or evidence of the reproducibility without undue experimentation of the claimed cells is required."

In response, Applicants submit that the amendment to claim 10 deleting the reference to the COP-5 cell, renders the Examiner's rejection moot with respect to these cells. Applicants further submit that the amendment to the specification at page 6, in the paragraph beginning on line 25, makes clear that the C127 cell line is deposited with the RIKEN depository and has been assigned accession no. RCB0036. Moreover, Applicants attach in Exhibit 3 the relevant pages obtained from the RIKEN web site, <http://www rtc riken go jp/CELL/HTML/RIKENCellBank html>, which indicate that the C127 cell line is deposited with RIKEN and is available to the public.

Applicants believe that the attached documents establish the public availability of the C127 cell line and overcome the Examiner's rejection. Therefore, Applicants respectfully request that the Examiner withdraw this ground of rejection.

**REJECTION OF CLAIMS UNDER 35 U.S.C. §102(b)**

The Examiner rejected Claims 2, 4, 5, 6 7 8 9 and 12 under 35 U.S.C. § 102(e) as anticipated by Pestka (U.S. Patent 6,300,474, filed 6/9/95). According to the Examiner, the claims "recite a nucleic acid that encodes a modified amino acid sequence with deletions and/or insertions and/or substitutions which [sic] the protein has antitumor activity, which is derived from Tricholoma matsutake and pBluescript SK(-) vector comprising the nucleic acid, E. coli host cell comprising a vector, and a method of producing the polypeptide. The Examiner further states that Pestka "teach the

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nucleic acid which encodes a protein that is an antitumor protein and vectors, host E.coli cells and methods of producing such proteins (see, columns 2, 4, line 48, 10, claims 2, 4, 9). The Examiner concludes that because "claim 1 recites the protein has one or more deletions, insertions, or substitutions, the art of Pestka reads on the claims."

In response, Applicants respectfully submit that the Examiner's rejection under §102(a) has been rendered moot by the cancellation of claim 1. Accordingly, Applicants respectfully request that the Examiner withdraw this rejection.

**REJECTION OF THE CLAIMS UNDER 35 U.S.C. § 103(a)**

The Examiner rejected claims 2, 4-9, and 12 under 35 U.S.C. § 103(a) as being unpatentable over Pestka (U.S. Patent 6,300,474) as applied to claims 2, 4-9, and 12 above, and further in view of Nagata et al (U.S. Patent 5,874,546). According to the Examiner, Pestka teaches as described above, and also teaches a wide variety of expression vectors and host systems for expression. The Examiner also states that Pestka does not teach JM109, but that this deficiency is made up for in the teachings of Nagata. The Examiner states that Nagata et al. teach nucleic acids, vectors, and host cells, especially JM109 cells. The Examiner concludes that it would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the JM109 cell of Nagata et al. with the nucleic acid of Pestka.

In response, and for the same reasons provided above, Applicants respectfully submit that the Examiner's rejection under 35 U.S.C. §103(a) is rendered

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moot by the amendments made herein to the claims. Claim 13 (formerly dependent claim 2) as re-presented recites a nucleotide molecule encoding a protein comprising the amino acid sequence of SEQ ID NO: 1. Pestka neither teaches or suggests such a nucleotide molecule, and this defect is not cured by the secondary reference of Nagata et al. Accordingly, Applicants respectfully request that the Examiner withdraw this rejection.

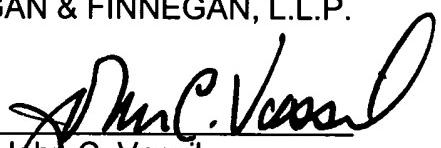
In view of the amendments and remarks above, Applicants respectfully request withdrawal of the Examiner's grounds of rejection and allowance of the pending claims.

The Commissioner is hereby authorized to charge any additional fees which may be required for this amendment, including all fees pursuant to 37 C.F.R. § 1.17 for its timely consideration, or credit any overpayment to Deposit Account No. 13-4500. Order No. 3479-4000US1. A DUPLICATE COPY OF THIS SHEET IS ATTACHED.

Respectfully submitted,

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